

# Use of Acthar GEL for MS Exacerbations During Natalizumab Induction and Maintenance

Ronald O. Bailey, M.D., Randy R. Heim, B.S., Vu A. Nguyen, M.A. and Carina G. Sprague, LVN



Riverside Medical Clinic, Riverside, CA

## OBJECTIVES

- Discuss safety and novel mechanism of action of ACTHar gel in the treatment of multiple sclerosis exacerbations during the concurrent use of natalizumab.

## BACKGROUND

- Natalizumab is a humanized recombinant monoclonal antibody interfering with the interaction of VLA-4 with its natural ligand VCAM-1 and fibronectin.
- Reduced extravasation of T and B cells through the blood brain barrier results, which creates an attenuated CNS inflammatory response.
- Natalizumab's contraindications include simultaneous use of immunosuppressive agents including Methylprednisolone, which may increase risk of PML.
- ACTHar gel represents an alternative medication for MS exacerbations.
- Because the mechanisms of action of ACTHar gel are believed to encompass melanocortin receptor activation, immunomodulation is potentiated with direct anti-inflammatory effects and immune effector cell modulation.

## METHODS

- Subjects who participated included MS patients (n=8) enrolled in the Touch Program and treated with natalizumab from three months to four years.
- Baseline EDSS scores ranged from 2.0-6.5. Clinical exacerbations were treated with a ten day course of ACTHar gel.
- In addition to Touch Program parameters, patients were evaluated with monthly blood work, monthly neurologic examinations, lumbar punctures performed yearly and following ACTHar administration and annual MRI scans. CSF immunologic profiles, JC virus DNA PCR probes in whole blood, urine and CSF, STRATIFY-1 JCV antibody testing, and NABs to natalizumab during and after exacerbations were obtained.

## RESULTS

- Four patients demonstrated JC seropositivity conversion (STRATIFY-1) and one demonstrated JCV DNA, PCR probe conversion in urine. JCV DNA PCR probes remained negative in whole blood and CSF of all patients enrolled in the study.
- Multiple natalizumab NAB testings were negative. Exacerbations occurred early and late in the course of natalizumab treatment and included: optic neuritis, ataxia and worsening myelopathy. No pseudoexacerbations were noted. EDSS scores improved following ACTHar gel administration.
- ACTHar gel side effects were minimal and included transient pedal edema. Stable parameters in CSF immunologic profiles, JCV DNA PCR in whole blood and CSF, and MRI study vectors were noted even in ACTHar treated patients even after four years of natalizumab use.

Figures 1 & 2. Patients MS Course Over Time

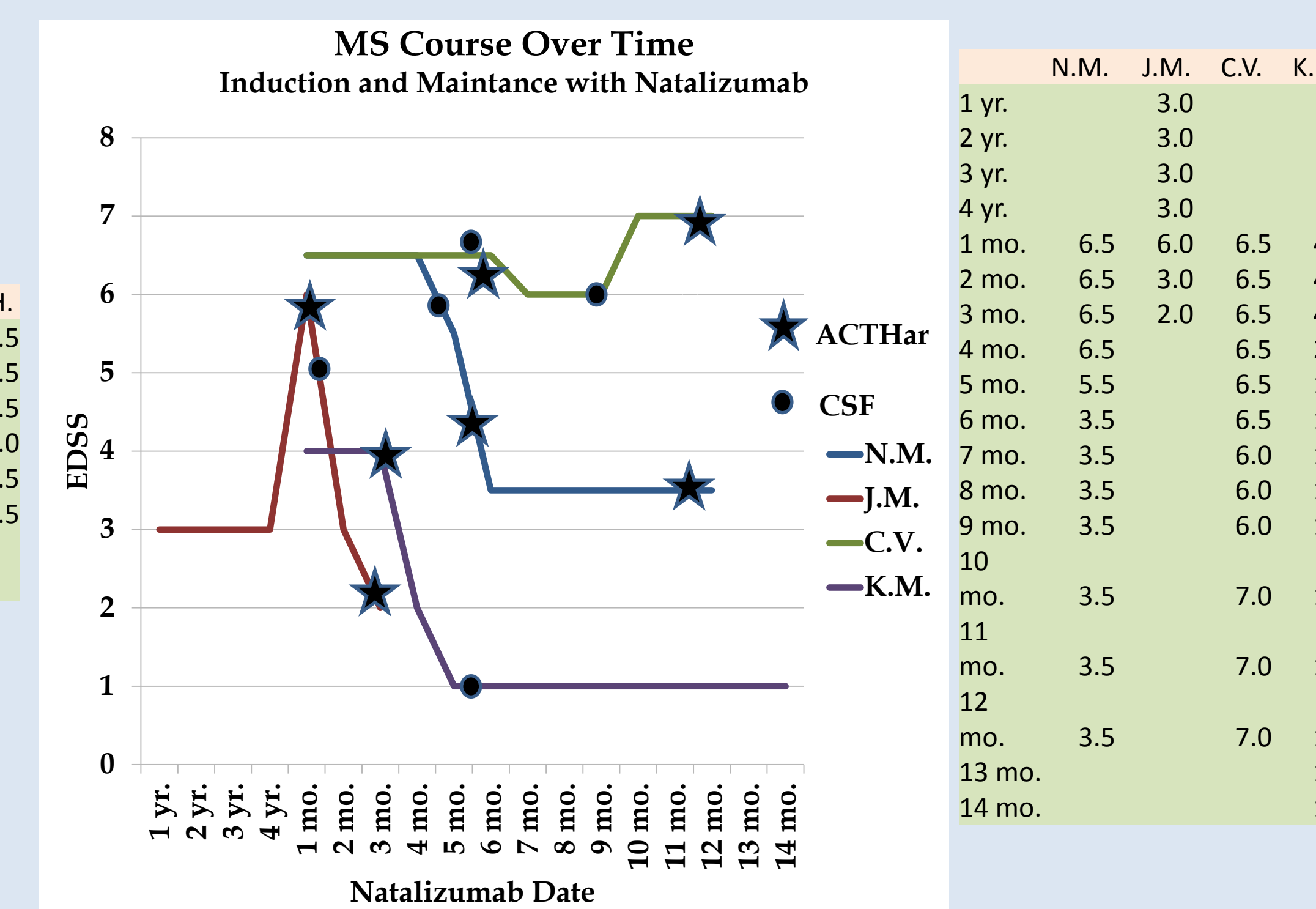
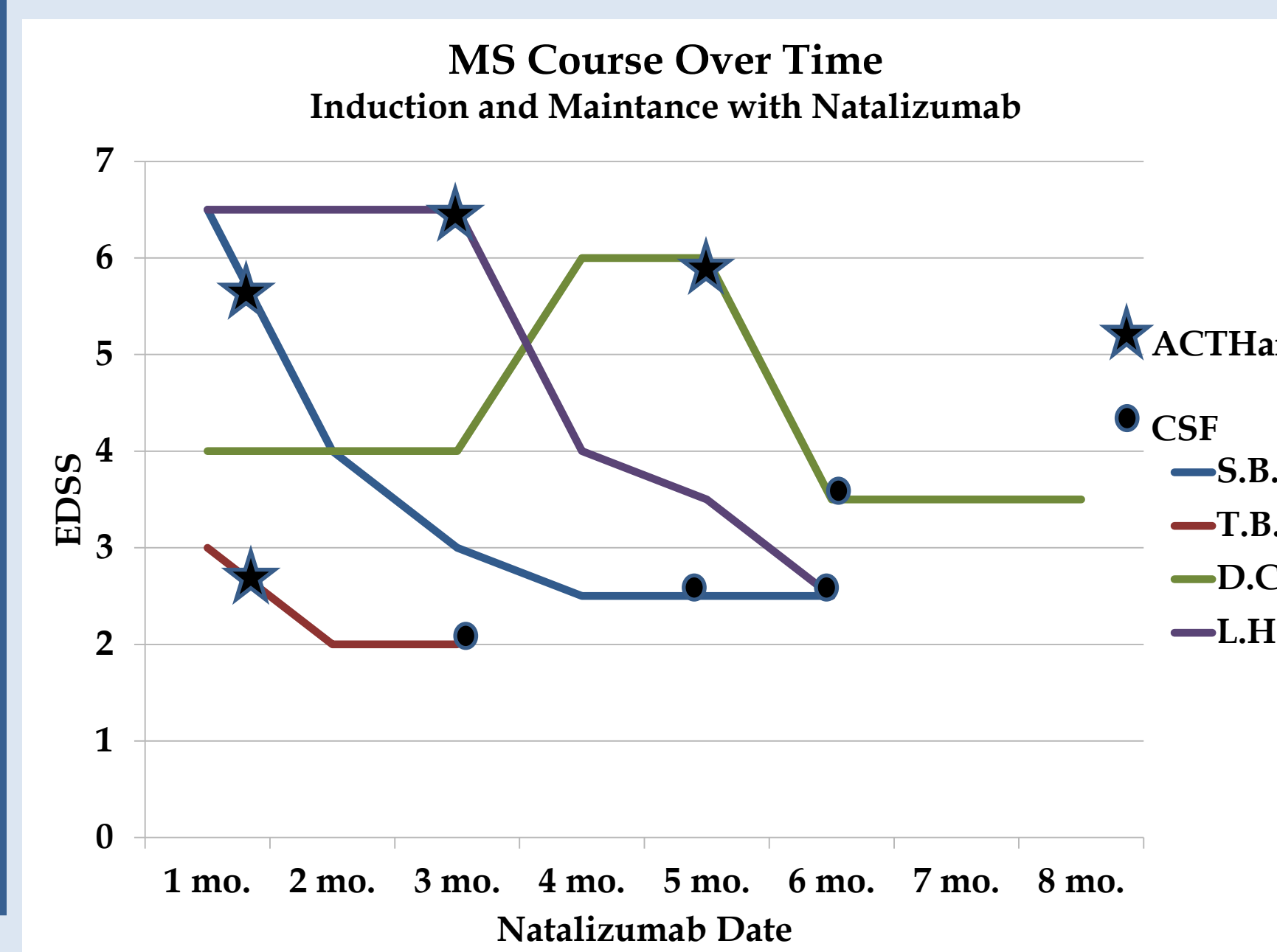


TABLE 1. Exacerbations on Natalizumab

Patient	EDSS	Symptoms/Signs at Time of Exacerbation*	Months on Natalizumab
S.B.	5.0	Worsening myelopathy	6
T.B.	2.0	Optic neuritis; incoordination	3
D.C.	3.5	Ataxia	8
L.H.	2.5	Myelopathy; optic neuritis	6
N.M.	3.5	Worsening myelopathy; Ataxia	12
J.M.	6.0	Worsening myelopathy; ?IRIS	48
C.V.	6.5	Worsening myelopathy; Appendicular-truncal ataxia	12
K.M.	6.5	Ataxia; Diplopia	14

\*No pseudoexacerbations

Table 2. Comparison of Stratify 1 (Elisa) serum, NABs to Natalizumab, JC Virus DNA, PCR

Patient	Stratify 1 (Elisa)	NAB Natalizumab	JC Virus DNA, PCR		
			Blood	Urine	CSF
S.B.	Positive @ 5 mo.	Negative	Negative	Negative	Negative
T.B.	Positive @ 3 mo.	Negative	Negative	Negative	Negative
D.C.	Negative @ 6 mo.	Negative	Negative	Negative	Negative
L.H.	Negative @ 6 mo.	Negative	Negative	Negative	Negative
N.M.	Negative @ 6 mo. Negative @ 12 mo.	Negative Negative	Negative Negative	Negative Negative	Negative Negative
J.M.	Positive @ 4 years Positive @ 4.3 years	Negative Negative	Negative Negative	Negative Negative	Negative Negative
C.V.	Positive @ 6 mo. Negative @ 12 mo.	Negative Negative	Negative Negative	Negative Positive	Negative Negative
K.M.	Negative @ 6 mo. Negative @ 12 mo.	Negative Negative	Negative Negative	Negative Negative	Negative Negative

## CONCLUSIONS

- Four patients demonstrated JC seropositivity conversion (STRATIFY-1) and one demonstrated JCV DNA, PCR probe conversion in urine. Treating MS exacerbations while on Natalizumab can be difficult. Immunosuppressive agents are contraindicated in use with Natalizumab.
- Based on our findings, ACTHar gel represents a safe and effective alternative medication. ACTHar induces endogenous production of cortisol and has direct effects on relapses via melanocortin receptors. Effects may be immunomodulatory rather than immunosuppressive, mitigating increased potential risk of PML.
- Patients who are JCV+ in serum (STRATIFY-1), may test negative for JCV DNA in blood, urine, and CSF over multiple time periods. In terms of DNA testing, urine was more sensitive compared to serum and CSF (the lowest numbers of viral copies are in CSF and the most are in urine).
- Future large scale studies are warranted to confirm our findings.

## ACKNOWLEDGEMENTS

The authors have nothing to declare.